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ABBREVIATIONS

ALL  acute lymphoblastic leukemia
AML  acute myeloid leukemia
CNS  brain tumors
NOPHO  Nordic Organization for Pediatric Hematology and Oncology
allogeneic  from a healthy donor
autologous  transplantation with the patient’s own cells
CML  chronic myeloid leukemia
MDS  myelodysplastic syndrome
NBL  neuroblastoma
NHL  non-Hodgkin lymphoma
SIB  HLA identical sibling
SAA  severe aplastic anemia
URD  unrelated HLA matched donor
TRM  transplant-related mortality, deaths related to recurrence of the disease excluded

Cover photo Kim Vettenranta. The picture shows leukemic cells.
Published in February 2015
UNIT INTRODUCTION

The Pediatric Hematology, Oncology and Stem Cell Transplantation Unit is Finland’s largest unit specialized in pediatric cancer care and hematological diseases, as well as allogeneic stem cell transplantation for children. The unit comprises the Pediatric Cancer Ward, a day hospital unit, a procedure unit, and an outpatient clinic.

The unit is responsible for the diagnosis and treatment of pediatric cancers and hematological diseases in its area. Additionally, the unit carries out all of Finland’s pediatric allogeneic bone marrow transplantations, and the respective training as part of specialization in pediatric hematology-oncology and stem cell transplantation. The unit also bears the key national responsibility for international cooperation in pediatric hematology-oncology as well as stem cell transplantation.

The unit covers all pediatric patients receiving stem cell transplantation, provides intravenous chemotherapy for pediatric cancer patients, and treats patients with benign hematological diseases as well as masters the respective diagnostics.

Staff at the unit includes six consultants in pediatric hematology-oncology and stem cell transplantation, a fellow in pediatric hematology-oncology as well as a pediatric anesthesiology consultant, a pediatric resident, more than 60 nurses, five ward clerks, as well as supportive staff including ward pharmacists, physical therapists, a rehabilitation coordinator, dietician, consultant in adolescent psychiatry, psychologist, social worker, kindergarten teacher, teacher, hospital pastor, instrument technician and ward domestics. All the consultants have an MD as well as a PhD degree, and three have a docent’s competence (equivalent to Assistant Professor) in pediatric hematology and oncology. In addition, at least two of the specialists will receive a docent’s competence in 2015.

The hospital sees approximately 5,000 in-patient days, 1,200 day clinic visits and 1,300 procedures that require anesthesia annually. There are approximately 4,000 outpatient clinic visits and around 1,000 home visits each year.

INTERNATIONAL/NORDIC RESEARCH AND TREATMENT PROGRAMS IN WHICH WE ALREADY PARTICIPATE, OR WHICH WE WILL BE JOINING IN 2015

Treatment programs in which we participate:
- Ewing’s sarcoma: Ewing 2008, Ewing-relapses
- Neuroblastoma: SIOPEN-HR-NBL 1.7
- Brain tumors: Angiocomb
- Allogeneic stem cell transplantation ALL SCTped FORUM 2012

Treatment programs that we are joining
- Brain tumors: PNET5 MB
CONVENTIONAL CANCER THERAPY

1. KEY FIGURES

Figure 1. Diagnosis distribution of new pediatric cancer cases in the years 2005-14. In 2014 58 new patients were admitted, 21 of whom had leukemia.

2. LEUKEMIAS

Figure 2. Treatment results in pediatric ALL and their development (Kaplan-Meier analysis). The rectangle at 5 years shows the respective, combined NOPHO result.
Figure 3. Treatment results in pediatric AML do not attain the level of those in ALL even on the international level, but in our unit are excellent. The new AML treatment protocol (AML-NBH-2012) has been launched in 2013 and the results have not yet matured. Again, the rectangle at 5 years gives the respective, combined NOPHO result for NOPHO-ALL-2004.

3. SOLID TUMORS

Figure 4. Diagnosis distribution of solid tumors in 2005-2014.
Figure 5. Cumulative survival for patients treated in four key diagnostic groups. The respective Nordic results (NOPHO) are, again, given at 5 years with the colored bars.

Figure 6. Cumulative survival for patients in three key brain tumor groups.
1. KEY FIGURES

A total of 439 allogeneic bone marrow transplants had been conducted and 333 cases of intensive chemotherapy followed by autologous stem cell rescue carried out at the Children’s Hospital by the end of 2014. This brings the total number of stem cell transplantations carried out by the end of 2014 to 772 including total of 39 cord blood stem cell transplantations.

2. ALLOGENEIC STEM CELL TRANSPLANTATIONS

Stem cell transplantations 2005-2014

Stem cell transplants from a healthy donor 2005-2014

- With the patient’s own cells
- From a healthy donor

- Register donor
- Relative donor
3. AUTOLOGOUS STEM CELL RESCUE

Figure 9. The indications for allogeneic transplantation in 2005-14 with the leukemias constituting up the largest single group.

Autologous stem cell indications 2005-2014

Figure 10. The diagnostic distribution of patients receiving autologous stem cell rescue with those with neuroblastoma constituting the largest single group.
KEY DATA FOR 2014

1. **Three** allogeneic stem cell grafts were harvested.
2. Autologous grafts were harvested for 7 patients, 6 times from bone marrow and **once** from peripheral blood.
3. A total of 10 donors were harvested.
4. The engraftment: **B-neut > 0.5 E9/l**

   **Allogeneic**
   - sib bm graft: median D +29 (min 12, max 31)
   - mud bm graft: median D +18.5 (min 12, max 30)
   - mud umbilical cord D +30
   - mud PBSC D +22
   **Autologous**: median D +16.5 (min 12, max 30)

In 2014 a total of 19 allogeneic and 4 autologous stem cell transplantations were carried out.

### Age and gender distribution of those receiving a transplantation

<table>
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<th>0-5 years</th>
<th>6-10 years</th>
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<tr>
<td><strong>Allogeneic</strong></td>
<td></td>
<td></td>
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<tr>
<td>boys 11, girls 8</td>
<td>6</td>
<td>5</td>
<td>8</td>
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<tr>
<td><strong>Autologous</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>boys 3, girls 1</td>
<td>3</td>
<td>1</td>
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### Indications for stem cell transplantation in 2013

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<td><strong>Allogeneic</strong> 19 cases</td>
<td>ALL 1. remission</td>
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</tr>
<tr>
<td></td>
<td>ALL &gt; 2 remission</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>AML 1. remission</td>
<td>4</td>
</tr>
<tr>
<td></td>
<td>SAA</td>
<td>3</td>
</tr>
<tr>
<td></td>
<td>Fanconi anemia</td>
<td>2</td>
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<tr>
<td></td>
<td>Hypoplastic anemia</td>
<td>1</td>
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<tr>
<td></td>
<td>JMML</td>
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</tr>
<tr>
<td></td>
<td>SCID</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>NHL</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Mutation that activates STAT3 gene</td>
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</tr>
<tr>
<td></td>
<td>HLH</td>
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<td><strong>Autologous</strong> 4 cases</td>
<td>Brain tumor</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>Neuroblastoma</td>
<td>2</td>
</tr>
</tbody>
</table>

Distribution of allogeneic stem cell transplantation patients according to university hospital district in 2014 and in 2005-14.
KEY RESULTS

Figure 11. Cumulative survival in allogeneic transplantation for ALL by donor type.

Figure 12. Transplant-related mortality (TRM) in ALL by donor type.
Figure 13. Cumulative survival in AML by remission status.

Figure 14. Cumulative survival in severe aplastic anemia by donor type.
SUMMARY

In 2014 our clinical ProLapsi database have been updated, e.g. to cover new patient groups (hematology and immunology) and the software (Filemaker®) has been upgraded.

In October 2014 we celebrated 40 years of stem cell transplantation at the Helsinki University Hospital Children's Hospital, the first allogeneic program to be launched in Finland and the Nordic countries.

As Finland's largest center the unit is responsible for the treatment of about 40% of the national total of pediatric cancer and hematological diseases. The doctors at the Children's Hospital are primarily responsible for the Finnish contribution to international cooperation (NOPHO, EBMT, other collaborative efforts). In the field of stem cell transplantation the unit is one of the three largest centers in the Nordic Countries, and medium-sized by European standards. The unit was the first pediatric center in the Nordic countries to receive the JACIE accreditation and remains the only one in Finland. The use of cord blood stem cells was initiated in 1994, again as the first in the Nordic countries. With currently 40 cord blood transplants completed, the Children's Hospital has an unparalleled experience in this field in the Nordic countries.

In October 2014 we underwent the JACIE (Joint Accreditation Committee of ISCT and EBMT) interim inspection with the next full inspection being due in late 2016.

Our results in the treatment of pediatric ALL and AML are of excellent international level and better than in the other Nordic Countries (c.f. figures 2 and 3). A new ALL treatment protocol (NOPHO ALL-2016) is under construction with one our consultants (Docent Mervi Taskinen) as its PI and the new AML treatment protocol (NOPHO-NBH-AML-2012) has recently been launched. Our unit has been shouldered the national responsibility for pediatric allogeneic stem cell transplantation in 2014 with our transplantation outcome in ALL being of good international level and that in AML of excellent international level (Figures 8-12).

In solid tumors our results are of excellent international level in lymphomas and nephroblastoma (Fig. 4). For neuroblastoma we joined the international SIOPEN-HR-NBL-1.5 treatment protocol in 2013, and thus justly expect a significant improvement in treatment results.

We will significantly intensify our international collaboration in the solid tumors in 2015-2016 by extensively joining European research and treatment protocols in at least lymphoma, soft tissue sarcomas, some brain tumors, and allogeneic stem cell transplantation for leukemia.

We also remain determined to develop our knowledge and skills: recently one of our Consultants underwent further training in the treatment of congenital immune deficiencies with stem cell transplantation (Great Ormond St. Children’s Hospital, London, autumn 2013). Another got further training in pediatric radiotherapy (HUS, autumn-winter 2014-2015) and a third is studying stem cell transplantation for hemoglobinopathies (Ospedale Pediatrico Bambino Gesu, Rome, spring of 2015). Our nurses also actively participate in national and international pediatric oncology and stem cell transplantation collaboration and training.

For the treatment of both acute and chronic graft-versus-host disease (GVHD) we have just recently (XI/14) launched an extracorporeal photochemotherapy program, the first pediatric program within the Nordic countries.

At the beginning of 2015, we will initiate the fourth two-year Clinical Nurse Specialist training program for pediatric hematology and oncology and stem cell transplantation in cooperation with outside collaborators in order to maintain and develop nursing expertise.

Furthermore, we aim at launching a national, pediatric diagnostics and treatment program for hemoglobinopathies.
Pediatric Hematology, Oncology and Stem Cell Transplantation Unit

K10 Pediatric Oncology Ward
Day hospital
Procedure unit
Outpatient clinic

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